

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2004/000349

A. CLASSIFICATION OF SUBJECT MATTER Int. Cl. ⁷ : C12Q 1/68 According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) See electronic database Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched See electronic database Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WPIDS, MEDLINE, CA, BIOSIS: TLR-2, TLR-4, toll like receptor, cirrhosis, hepatocellular carcinoma, HCC, HepC, HepB, HCV, HBV, hepatitis, virus, viral, disease, diagnos?, treat?, prognosis		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Manigold <i>et al.</i> (2003) 'Differential expression of toll-like receptors 2 and 4 in patients with liver cirrhosis' European Journal of Gastroenterology & Hepatology Vol 15(3): 275-282	1, 2, 4, 6, 10-14, 16, 21-24, 26, 28, 32-36, 38, 43-47, 49, 54-64
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "I" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family	
Date of the actual completion of the international search 28 June 2004		Date of mailing of the international search report 02 JUL 2004
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaaustralia.gov.au Facsimile No. (02) 6285 3929		Authorized officer LEXIE PRESS Telephone No : (02) 6283 2677

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Manigold <i>et al.</i> (1999) 'Upregulation of toll-like receptor-2 in patients with liver cirrhosis' Hepatology Vol 30(4) Part 2: 434A	1, 2, 4, 6, 10-14, 16, 21-24, 26, 28, 32-36, 38, 43-47, 49, 54-64
X	O'Neill L. (2000) 'The toll/interleukin-1 receptor domain: a molecular switch for inflammation and host defence' Biochemical society Transactions Vol 28(5): 557-563	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
X	WO 2001/36488 A1 (LEIV EIRIKSSON NYFOTEK AS) 25 May 2001 (see in particular page 1, lines 1-6; claims 26 and 30)	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Paik <i>et al.</i> (2003) 'Toll-like receptor 4 mediates inflammatory signaling by bacterial lipopolysaccharide in human hepatic stellate cells' Hepatology Vol 37(5): 1043-1055	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Riordan <i>et al.</i> (2003) 'Peripheral blood mononuclear cell expression of toll-like receptors and relation to cytokine levels in cirrhosis' Hepatology Vol 37(5): 1154-1164	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Riordan <i>et al.</i> (2003) 'Toll-like receptor expression in cirrhosis' Gut Vol 52 No. Suppl. 1: A2	1,2, 6, 8-14, 19-24, 28, 30-36, 41-46, 52-64
P, X	Visvanathan <i>et al.</i> (2003) 'Up-regulation of toll-like receptor expression in chronic hepatitis C: correlation with circulating pro-inflammatory cytokine levels and hepatic necro-inflammatory activity' Gut Vol 52 No. Suppl. 1: A35	1-3, 6, 10-15, 21-25, 28, 32-37, 43-48, 54-64
P, X	Visvanathan <i>et al.</i> (2003) 'Impaired toll-like receptor expression in chronic hepatitis B' Gut Vol 52 No. Suppl. 1: A36	1, 2, 6, 7, 10-14, 18, 21-23, 29, 32-36, 40, 43-47, 51, 54-64

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.: **45-64 in part**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

see extra sheet
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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Supplemental Box

(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: II.2

Present claims 45 to 64 refer to a large number of possible agents and their use. These agents are defined by a desirable property namely, antagonist/agonist or regulator of TLR-2 or TLR-4. The claims cover all substances and compounds having this property, whereas the application does not provide support within the meaning of Article 6 PCT for any specific example of such substances or compounds. Because the claims lack support, no meaningful search encompassing their entire scope is possible.

The Applicant's attention is drawn to the fact that claims relating to inventions in respect of which no International Search has been established need not be the subject of an International Examination.

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END OF ANNEX